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Cardiac Behçet's Disease Presenting with Right Ventricular Endomyocardial Fibrosis and Intracardiac Thrombosis: a Case Report

Eun Ji Choi[1], Min Sun Kim[1], Hyun Jung Koo[1], Jae-Kwan Song[2], Joo Seon Song[3], Joon-Won Kang[1], Dong Hyun Yang[1]

[1]Department of Radiology and Research Institute of Radiology, Asan Medical Center, Seoul, Korea
[2]Division of Cardiology, Cardiothoracic Imaging Center, Asan Medical Center, Seoul, Korea
[3]Department of Pathology, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea

Case Report

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Correspondence to:
Hyun Jung Koo, M.D., Ph.D.
Department of Radiology and Research Institute of Radiology, Cardiothoracic Imaging Center, Asan Medical Center, 88 Olympic-ro 43 gil, Songpa-gu, Seoul 05505, Korea.
Tel. *** - **** - ****
Fax. +82-2-3010-2768
E-mail: radkoo@amc.seoul.kr

Behçet's disease is a chronic inflammatory disorder involving vessels of various sizes and organs, including the skin, joints, gastrointestinal tract, lungs, and cardiovascular system. The etiology of Behçet's disease is unclear, and clinical diagnosis is important in the absence of definitive laboratory or pathological findings diagnostic of Behçet's disease. Cardiac involvement is rare but might present as endocarditis, myocarditis, pericarditis, or intracardiac thrombosis. This report presents a case of Behçet's disease involving the heart in a 22-year-old man with unusual manifestations of right ventricular fibrosis and intracardiac thrombosis. Cardiac magnetic resonance imaging revealed multiple intracardiac thrombi and delayed diffuse subendocardial enhancement involving the right ventricle. No peripheral eosinophilia was detected. Endomyocardial biopsy showed mixed inflammatory cell infiltrates. Based on the patient's clinical history of oral ulcer and arthritis, a diagnosis of Behçet's disease was made considering the clinical, radiological, and histological findings. Intracardiac thrombi and endomyocardial fibrosis are rare manifestations of Behçet's disease, and the diagnosis is often a clinical challenge. Early diagnosis is important for appropriate management. Behçet's disease should be considered in the differential diagnosis of patients with intracardiac thrombosis and endomyocardial fibrosis of the right chamber.

Keywords: Behçet's disease; Intracardiac thrombosis; Endomyocardial fibrosis; Magnetic resonance imaging

INTRODUCTION

Behçet's disease is a chronic inflammatory disorder characterized by oral and genital ulcers, skin lesions, and uveitis. The etiology is unclear; however, it is considered as a systemic vasculitis involving vessels of any size. It may also involve various organs, such as the gastrointestinal tract, joints, central nervous system, and cardiovascular system (1, 2). Cardiac involvement is rare, and is reported in 1-6% of the patients with Behçet's disease (3, 4). Cardiac manifestations include pericarditis, myocarditis, endocarditis,

endomyocardial fibrosis, coronary arteritis, and intracardiac thrombi (4). Due to the lack of specific diagnostic laboratory tests and histopathologic findings, the diagnosis of the disease is based on clinical criteria (5). This report describes the case of a patient with Behçet's disease who presented with right ventricular (RV) fibrosis and intracardiac thrombi, which are rare manifestations of this disorder.

CASE REPORT

A 22-year-old man visited a general hospital with symptoms of swelling, erythema, and tenderness below both knees. A case of cellulitis was suspected, and the patient was administered intravenous antibiotics. One month later, he visited a tertiary care hospital with symptoms of mild fever, cough, and dyspnea on exertion. Initial laboratory results showed elevated concentrations of C-reactive protein (5.04 mg/dL), D-dimer (5.39 μg/mL), and fibrinogen (524 mg/dL), and an elevated erythrocyte sedimentation rate (94 mm/h). The platelet counts (180 × 10^3/μL) and antinuclear antibody titer were within normal limits, and lupus anticoagulant was negative. His white blood cell count (WBC) was mildly elevated (11.2 × 10^3/μL), but the peripheral eosinophil count was 0.3%, below the normal range of 1-7%. No pathogens were identified in blood culture.

These results led to a suspicion of pulmonary infection or thromboembolism. Chest computed tomography (CT) showed pulmonary thromboembolism involving the anterior and lateral basal segmental pulmonary arteries of the right lower lobe. Although it was a non-electrocardiography gated CT, low-attenuation soft-tissue lesions were noticed along the RV, and mass or RV papillary muscle thickening was detected (Fig. 1). Initial echocardiography showed diffuse thickening of the RV wall and echogenic mass or thickening of the RV papillary muscle (Fig. 2 and Supplementary video 1). Despite intravenous heparin injection (25,000 IU), trans-esophageal echocardiography performed 5 days later revealed persistent and diffuse thickening of the RV wall and echogenic mass or thickening of the RV papillary muscles.

RV endomyocardial fibrosis was suspected, and hence, contrast-enhanced cardiac magnetic resonance (CMR) imaging using 1.5-T Avanto (Siemens Healthcare, Erlangen, Germany) was performed. Four-chamber cine images demonstrated multiple mobile intracardiac soft tissues attached along the RV and RV outflow tract wall and thickened papillary muscle. Interventricular septal straightening with D-shaped left ventricle was noted; however, RV contractility was preserved (Supplementary video 2). Late gadolinium enhancement (LGE) images showed multifocal dark signal intensity representing intracardiac thrombi in the RV, with the largest thrombus measuring 2.8 cm in length, accompanied by multiple small thrombi along the RV wall and outflow tract. The entire RV wall and outflow tract showed diffuse thickening and delayed subendocardial enhancement (Fig. 3). Based on these findings, our initial impression was eosinophilic myocarditis or endomyocardial fibrosis.

An endomyocardial biopsy was performed. Histopathological evaluation revealed mixed inflammatory cell infiltrates, and Behçet's disease involving the heart was suspected. Further clinical history was obtained; however, no other symptoms were detected similar to those included in the diagnostic criteria for Behçet's disease, such as oral or genital aphthosis. However, the patient reported a pulmonary thromboembolic event and a history of recurrent joint pain in both knees. Arthritis is not included in the diagnostic criteria but is a common manifestation of Behçet's disease. Brain magnetic resonance angiography and CT angiography of the lower extremities revealed no definitive thrombosis or other vascular manifestations in the brain or lower extremities. The patient was treated with warfarin 1.5 mg/day and prednisolone 40 mg/day for 2 months on suspicion of Behçet's disease. He developed recurrent oral ulcer 5 months after the initial day of hospital visit during follow-up. He has been followed up regularly for the management of suspected Behçet's disease at a local tertiary care hospital. The medical records revealed a decrease in mass-like lesions within the RV but a persistent linear mass attached to the RV apex was detected via echocardiography performed 5 months after treatment with warfarin and prednisolone.

DISCUSSION

Cardiac involvement in Behçet's disease is very rare and is characterized by pericarditis, endomyocardial fibrosis, coronary artery disease, myocardial dysfunction, valve dysfunction, periaortic pseudoaneurysm, and intracardiac thrombus (3, 4). Cardiac thrombosis and endomyocardial fibrosis are rarer forms of cardiac involvement, and reported in 19.2% and 7.7% of the 52 patients diagnosed with cardiac Behçet's disease, respectively (4).

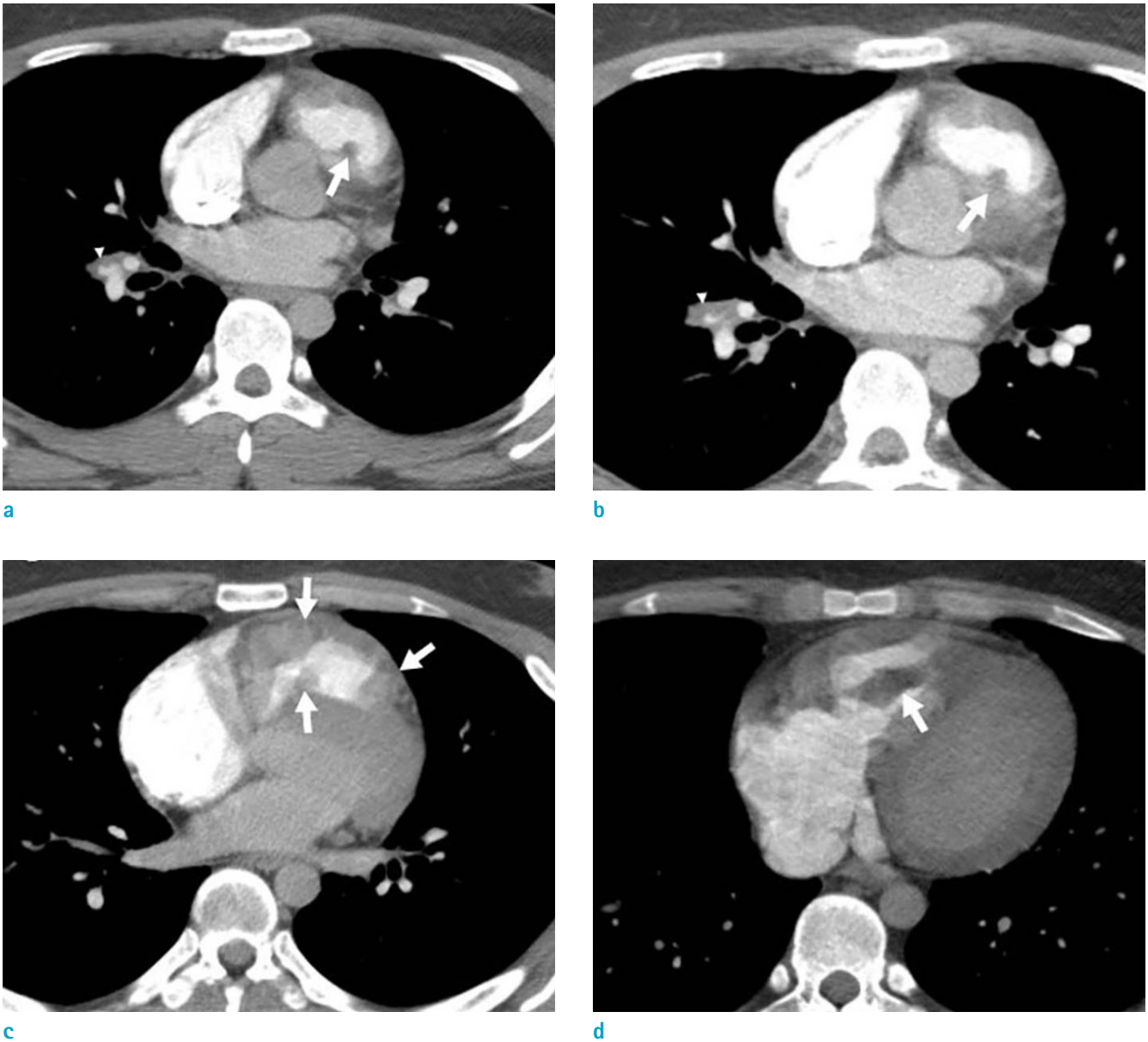

Fig. 1. (a-c) Contrast-enhanced axial chest computed tomography (CT) images show a low-attenuation filling defect in the anterior and lateral basal segmental pulmonary arteries of the right lower lobe, suggestive of pulmonary thromboembolism (arrowheads). In addition, multiple low-attenuation soft tissue lesions along the right ventricle (RV) and walls of the RV outflow tract (arrows) are seen. (d) RV papillary muscle thickening or mass attached to the papillary muscle (arrow) is also visible.

Endomyocardial fibrosis may be attributed to vasculitis involving the endocardium or myocardium or both, and complicated with intraventricular thrombosis. Right-sided chambers, especially the RV are the most frequent sites of involvement. Histological findings are not specific for cardiac manifestations of Behçet's disease but can be used to establish the diagnosis based on thrombi and dense fibrous tissue with mixed inflammatory cell infiltrates, which are associated with vasculitis.

However, the pathogenesis of thrombus formation in Behçet's disease is still unclear. Behçet's disease is considered a procoagulant state, with elevated fibrinogen and activator inhibitor type 1 concentrations, without involving the platelets (6). The levels of genetic

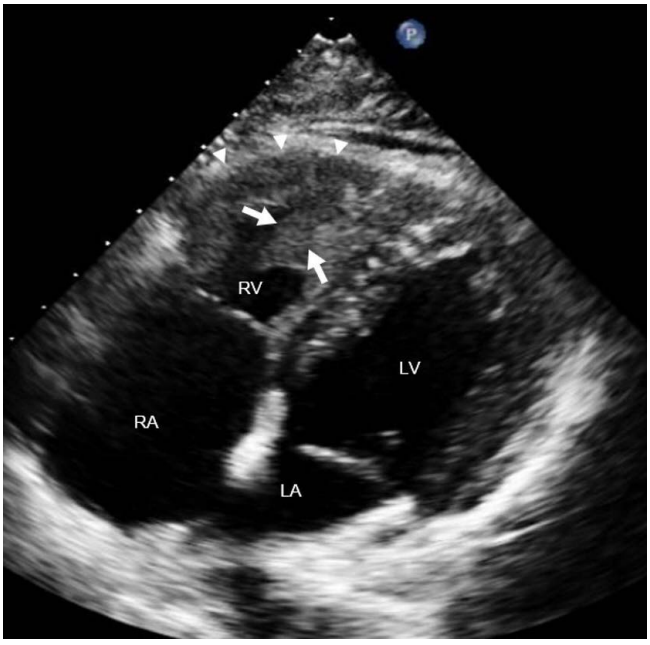

Fig. 2. Apical four-chamber transthoracic echocardiography reveals diffuse thickening (4-5 mm) of the RV wall with an echogenic layer (arrowheads). An approximately 1 cm intraventricular echogenic mass or thickened RV papillary muscle is observed within the RV (arrows). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

prothrombotic factors, including Factor V Leiden and prothrombin 20210 G-A gene mutations, are increased in Behçet's disease, and these factors might lead to thrombosis (7). In addition, endomyocardial fibrosis involving the right side of the heart might play a role in intracardiac thrombosis (8).

Imaging findings of endomyocardial fibrosis usually appear as a bright echo on echocardiography or low-CT attenuation along the myocardium. The most distinctive morphologic feature is the apical obliteration of the RV associated with enlarged right atrium. CMR with LGE revealed subendocardial enhancement, not restricted to any coronary territory. Although the role of CMR in Behçet's disease has yet to be established, it can be used to delineate cardiac anatomy, lesion characterization, and ventricular function. Additionally, LGE images play an important role in the diagnosis of cardiac involvement of Behçet's disease by revealing the presence and pattern of myocardial inflammation, injury, and fibrosis.

The differential diagnosis of subendocardial enhancement involving the right chamber should include endomyocardial fibrosis and eosinophilic myocarditis. Endomyocardial fibrosis is a form of restrictive cardiomyopathy and an idiopathic disorder. Imaging findings of idiopathic endomyocardial fibrosis and late-stage eosinophilic myocarditis (Löffler endocarditis) are similar to those of endomyocardial fibrosis associated with the cardiac manifestation of Behçet's disease. It is difficult to distinguish between these diseases without evaluating the clinical manifestations and laboratory findings. Idiopathic endomyocardial fibrosis is a diagnosis by exclusion. Eosinophilic myocarditis is currently considered as a manifestation of hyper-eosinophilic syndrome. In contrast to eosinophilic myocarditis, Behçet's disease is not characterized by eosinophilia. Further, eosinophilic myocarditis is histologically characterized by the presence of eosinophils or evidence of eosinophilic degranulation, whereas Behçet's disease involves mixed-cell infiltrations. A sample of fibrotic tissue obtained by endomyocardial biopsy in our patient failed to detect eosinophilia. Other ancillary findings such as aneurysm of the sinus of Valsalva, periaortic pseudoaneurysm, pulmonary artery aneurysm, or pulmonary thromboembolism represent important diagnostic clues.

The major criteria for the diagnosis of Behçet's disease based on the International Criteria for Behçet's Disease (ICBD) scoring system include oral aphthosis, genital aphthosis, skin lesions, and ocular lesions. The only minor criteria included in the ICBD scoring system are vascular lesions and involvement of the central nervous system. Although the ICBD scoring system does not include other symptoms and signs of arthritis, gastrointestinal lesions, and epididymitis, arthritis has been detected in 33-93% of patients with Behçet's disease (9). Further, symptoms and signs of arthritis are regarded as the most common minor manifestations of Behçet's disease (9). There is no consensus regarding the treatment of cardiac manifestations of Behçet's disease, usually presenting as intracardiac thrombi. Medical treatments to date include colchicine, corticosteroids, immunosuppressants, and anticoagulants. Immunosuppressants are considered the treatment of choice for vasculitis, with no difference in the recurrence rates of thrombosis between patients treated with immunosuppressants alone (e.g., azathioprine, mycophenolate, or cyclosporine) or immunosuppressants combined with anticoagulants (10). Cardiac surgery might be the next step for management of cases involving extensive or recurrent intracardiac thrombosis intractable to medical treatment.

This case report demonstrates a rare cardiac manifestation of Behçet's disease, presenting with large RV thrombi and

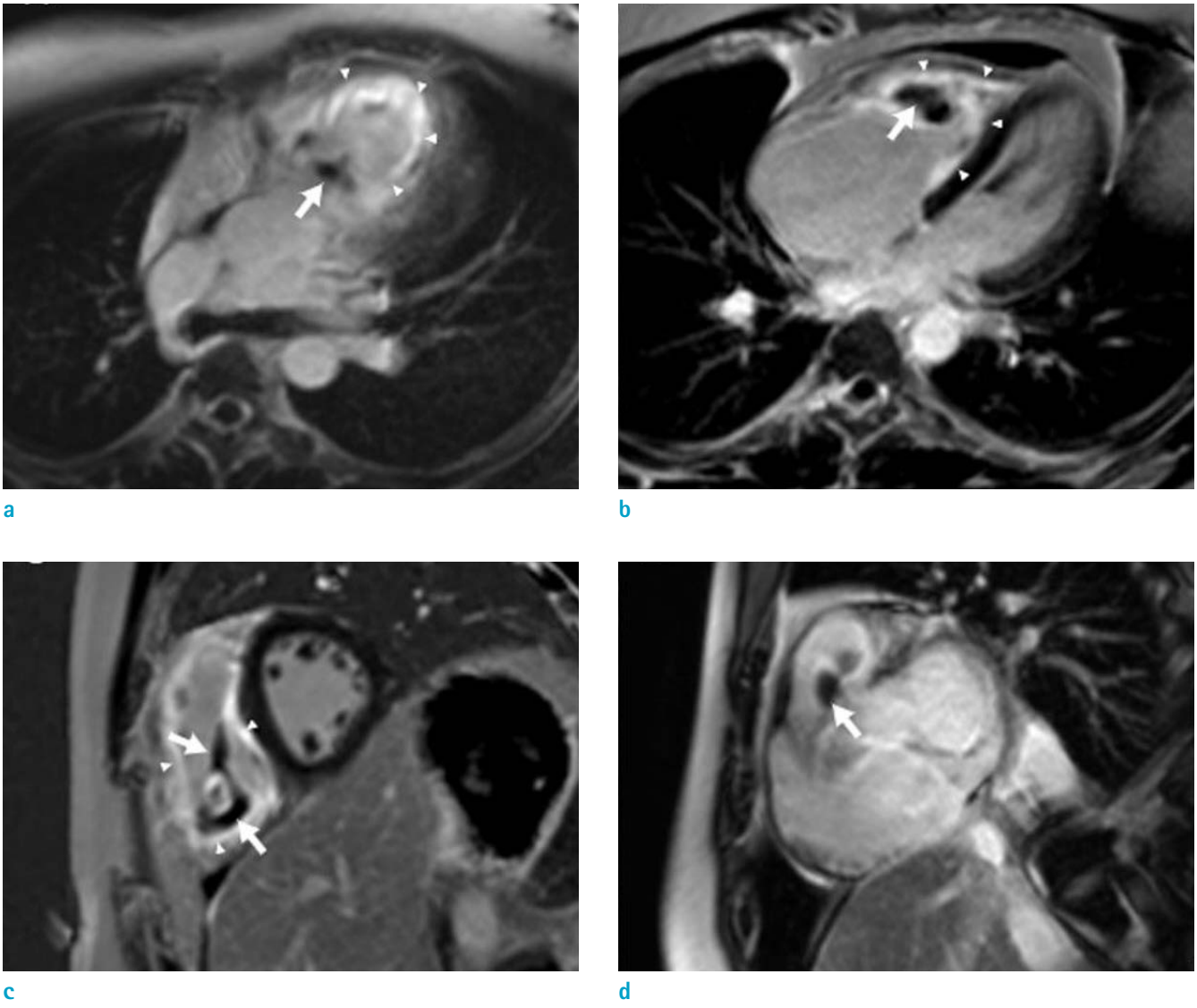

Fig. 3. (a-d) Four-chamber and short-axis late gadolinium-enhanced MR images show multifocal intracardiac thrombi of dark signal intensity in the right ventricle (RV). The largest thrombus is 2.8 cm in length (arrow in b), accompanied by multiple small thrombi along the RV wall (arrows in c) and RV outflow tract (arrows in a, d). Diffuse thickening and subendocardial delayed enhancement is also observed in the entire RV and the RV outflow tract (arrowheads in a, b, c).

extensive RV endomyocardial fibrosis on initial imaging. Behçet's disease is diagnosed based on the combination of clinical and CMR findings.

Supplementary Materials

The Video Supplements are available with this article at https://doi.org/10.13104/imri.2021.25.4.332

REFERENCES

1. Escudier M, Bagan J, Scully C. Number VII Behcet's disease (Adamantiades syndrome). Oral Dis 2006;12:78-84
2. Sakane T, Takeno M, Suzuki N, Inaba G. Behcet's disease. N Engl J Med 1999;341:1284-1291
3. Lee I, Park S, Hwang I, et al. Cardiac Behcet disease presenting as aortic valvulitis/aortitis or right heart inflammatory mass: a clinicopathologic study of 12 cases. Am J Surg Pathol 2008;32:390-398
4. Geri G, Wechsler B, Thi Huong DL, et al. Spectrum of

cardiac lesions in Behcet disease: a series of 52 patients and review of the literature. Medicine (Baltimore) 2012;91:25-34
5. International Team for the Revision of the International Criteria for Behcet's Disease (ITR-ICBD). The International Criteria for Behcet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol 2014;28:338-347
6. Fernández-Bello I, López-Longo FJ, Arias-Salgado EG, Jiménez-Yuste V, Butta NV. Behcet's disease: new insight into the relationship between procoagulant state, endothelial activation/damage and disease activity. Orphanet J Rare Dis 2013;8:81
7. La Regina M, Orlandini F, Prisco D, Dentali F. Homocysteine in vascular Behcet disease: a meta-analysis. Arterioscler Thromb Vasc Biol 2010;30:2067-2074
8. Mogulkoc N, Burgess MI, Bishop PW. Intracardiac thrombus in Behcet's disease: a systematic review. Chest 2000;118:479-487
9. Davatchi F, Shahram F, Chams-Davatchi C, et al. Behcet's disease: from East to West. Clin Rheumatol 2010;29:823-833
10. Ahn JK, Lee YS, Jeon CH, Koh EM, Cha HS. Treatment of venous thrombosis associated with Behcet's disease: immunosuppressive therapy alone versus immunosuppressive therapy plus anticoagulation. Clin Rheumatol 2008;27:201-205